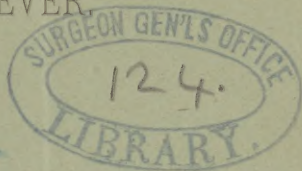


*With the Author's Compliments.*

SMYTHE (G.C.)

THE  
ANTIPYRETIC TREATMENT  
OF  
TYPHOID FEVER.

BY



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A Paper read before the Medical Society of the Missis-  
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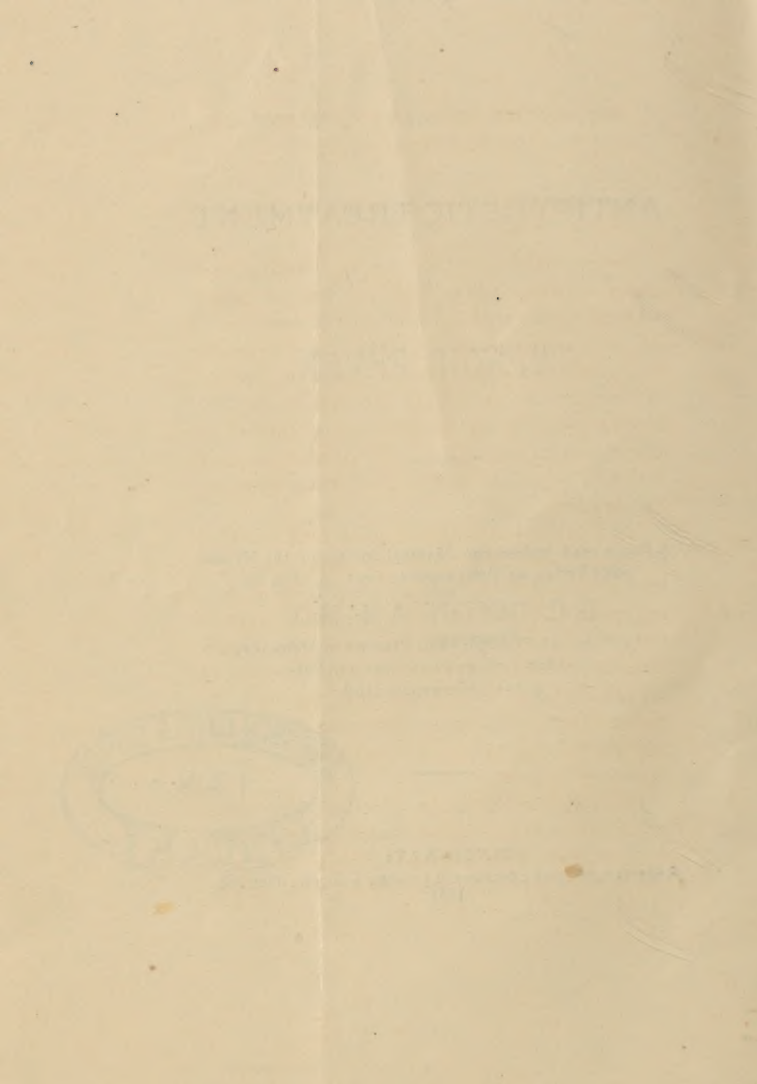
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## THE ANTIPYRETIC TREATMENT OF TYPHOID FEVER.

BY G. C. SMYTHE, A.M., M.D.

Under the rules of your society, limiting each paper to twenty-five minutes, it will be impossible to discuss the subject of typhoid fever in its entirety, consequently I shall confine my remarks exclusively to its treatment, or rather to one particular plan of treatment, the antipyretic, discussing the pathology and symptomatology of the disease, so far only as may be necessary to furnish a rational basis for the plan which I propose to advocate.

Death may result in this disease from a variety of causes depending upon the nature and extent of the structural lesions, which take place in any given case. These lesions are very properly divided into *primary* and *secondary*, the former including the local hyperæmia which occurs in the mucous membrane of the small intestine, together with the infiltration, softening and sloughing of the solitary and agminated glands with the subsequent ulceration.

These with some changes of minor importance, which take place in the mesenteric glands, spleen, etc., are the specific lesions of typhoid fever, and owe their origin to the direct effects of the poison,

and are as necessary to the existence of a typical case as are the eruptions in the exanthemata or the specific lesions which occur in any of the infectious diseases. Death may take place from these structural changes. The necrobiotic processes in Peyer's patches may open blood-vessels sufficiently large to cause death from hemorrhage, or perforation may take place followed by a fatal peritonitis.

Only a small percentage of the mortality of this disease however can be charged to the specific lesions. Tabulating all the statistics to which I have had access, I find that less than six per cent. of the total number of cases have hemorrhage; of these a little less than one-third die, or less than two per cent. of the whole. About one per cent. of the totality of cases has perforation of the bowel, and a small portion of these recover, so that the entire mortality of this disease, arising from the specific lesions, is not far from three per cent.

It is plain then that we must look to the group of secondary lesions or those caused by the general disease for the cause of the heavy mortality in typhoid fever. These structural changes do not belong exclusively to this disease, but may occur in any disease *characterized by persistent elevation of temperature*, to which they undoubtedly



owe their origin. They consist of congestions, inflammations and degenerations of important organs, and may include any organ or tissue in the body.

Death may result from the sudden arrest of function of some important organ or organs as the heart, brain, or lungs, without the structural changes just mentioned, but be caused by the effect of elevation of temperature sufficient to *produce paralysis of these organs.*

Then we may have a fatal result occurring from three different sources in this disease.

1st. From the effects of the primary or specific lesions, ulcerations, hemorrhage and perforation.

2nd. Directly from the effects of hyperpyrexia producing paralysis of heart, lungs or brain.

3rd. Indirectly, by the pathological changes in important organs caused by the persistent elevation of temperature.

It is now a well established fact that the characteristic symptoms of typhoid fever such as low muttering delirium, picking at imaginary objects, sliding down in bed, subsultus tendinum, sordes, etc., are not the direct result of the specific poison of the disease, but rather the effect of the long continued elevation of temperature during which the structure and functions of important organs are effected by the heat, and the circula-

tion is *poisoned by the detritus of rapidly oxydized tissue*, which accumulates more rapidly than it can be eliminated; this group of symptoms, known as the *typhoid condition*, occurs in all diseases which are characterized by persistent elevation of temperature, such as typhus, yellow, and scarlet fevers, small-pox, measles, and even malarial fevers, when they become continued; under any and all circumstances these symptoms owe their origin to continued hyperpyrexia.

The mortality of typhoid fever *varies* greatly in different epidemics and in different countries. It is exceedingly difficult to arrive at a satisfactory conclusion in regard to the exact death-rate. In the French Army from 1875 to 1880 inclusive, in 26,000 cases the death-rate was over 36 per cent. German statistics under the expectant plan of treatment which was used prior to 1862, gave a mortality of about 28 per cent.; the English and American death-rate is somewhat lower, but it will be safe to state without wading through long columns of dry figures, that the percentage of deaths tabulated from the statistics of the entire civilized world would be somewhere between 25 and 30 per cent. Less than five per cent. of these deaths are shown to be caused by the specific lesions of the fever, and the remaining 20 or 25 per cent. of deaths are due to the



secondary lesions, and are caused by the long continued pyretic condition present in the disease and *can, and ought to be prevented by antipyretic treatment.*

The etiology of typhoid fever is imperfectly understood, but modern investigation however has a tendency to establish the truth of what has been discussed for ages as the germ theory, and the probabilities are that the causes of all the infectious diseases will be ultimately traced to low living vegetable organisms.

We possess no specifics for the disease in the same sense that quinia is a specific for malarial diseases or that salicylic acid and its salts are specifics for acute articular rheumatism; so we are compelled to adopt a symptomatic treatment, to combat unpleasant and dangerous symptoms and see that the patient does not die from complications, inter-current diseases or sequelæ.

These objects are best subserved by the cooling treatment. The temperature in this disease controls the situation. The danger is proportionate to its height and persistency, and although the hyperpyretic condition is never free from danger however brief its duration (for death may take place in a few hours from paralysis of heart or brain), it is to its *persistency* that the danger in this disease owes its origin. A temperature of

103° or 104°, which is persistent for a period of three or four weeks will work more pathological mischief than a temperature of 106° or 107°, which remits promptly, as in malarial and relapsing fevers.

Statistics show that with a purely expectant treatment, where the temperature did not reach 104°, in typhoid fever, the mortality was about 9 per cent.; where it passed 104°, but did not reach 105° the mortality was about 29 per cent.—when it passed 105° but did not reach 106° the death-rate exceeded 50 per cent.; and where it passed 107° recovery was rare. In all febrile diseases one of two factors is present and in a majority of cases both; they are, 1st, excessive heat production, and, 2nd, faulty heat elimination. Antipyretic treatment consists in the administration of medicine to prevent this excessive production;—and the energetic application of cold water and other means to hasten its elimination by abstraction.

In order to accomplish the best possible results by this plan of treatment it must be *begun early and persisted in until the danger is passed*. This is a four weeks' fever. During the first week there is a gradual but persistent elevation of temperature, at the close of which in a vast majority of cases the maximum is reached, the

temperature then is persistent with slight diurnal variations until the latter part of the third week or beginning of the fourth when the disease begins to decline, and the temperature is characterized by daily remissions of several degrees. If this period is reached without any serious complication or intercurrent disease arising from excessive heat, the patient ought to recover unless death takes place from the specific lesions of the disease, the manner of which has been already discussed.

In the application of cold water as a therapeutical agent, we are using a means of great power, and one that must be used with care or harm may follow. An agent that will lower the temperature in febrile conditions four or five degrees in ten or fifteen minutes, accomplishing this by actual abstraction of heat is not intended for the amusement of the patient and his friends, while nature cures the disease.

In applying all thermo-therapeutical remedies, we should be guided largely, if not solely, by the revelation of the clinical thermometer. This instrument was introduced into clinical medicine by Dr. Antonius de Haen, of Vienna, in 1754, but did not attract the attention it merited. Dr. James Currie of Liverpool, again brought it into notice in 1797, but the profession, always slow to

indorse great improvements and new discoveries, failed to recognized its importance until nearly three quarters of a century later. I regard the revival of clinical thermometry with its daily application at the bedside of more importance to the sick than any improvement of the 19th century.

Heat may be abstracted by affusion, immersion, the cold pack, sponging, or the use of Kibbee's cot. Affusion is the most effective, but is most unpleasant to the patient. This is Dr. Currie's method as described in his work, published in England in 1797. He claimed that typhus fever could be aborted by this means and that scarlet fever and small-pox were rendered mild and tractable affections. His method consisted in dashing upon the naked body of the patient five or six gallons of cold water, the temperature of which was, in some cases which he reports with full particulars, as low as  $44^{\circ}$  Fahr. This process was always followed by a rapid reduction of temperature sometimes reaching the normal. I have used the cold affusion in malarial and scarlet fevers with the same happy effect described by Dr. Currie. I have treated one case only of typhoid fever in this way of which I shall speak more fully presently.

I am convinced however, after a somewhat extended trial of these different methods of abstrac-

tion, that what is known as the graduated bath of Von Ziemssen is most suitable for a majority of cases, and this is especially so for children and old people, because the shock of this bath is much less to the patient, and if properly applied the abstraction is none the less perfect. Fifteen or twenty gallons of water, a Knowlton's portable rubber bath-tub, a clinical and an ordinary thermometer, are all the implements necessary to administer these baths. The same water can be used if necessary for several immersions. The patient should be immersed at full length in the water, the temperature of which should be about ten degrees lower than that of his body, and after remaining two or three minutes, cold water should be added gradually until the temperature of the fluid in the tub is reduced to  $70^{\circ}$  or even  $65^{\circ}$  in obstinate cases. From fifteen to twenty minutes will be required to reduce the temperature of the patient to one hundred or below; while plunging him into cold water of  $60^{\circ}$ , according to the method of Liebermeister, will accomplish the reduction in ten or twelve minutes, but is much more unpleasant to the patient. The effect of a bath is to lower the pulse and respiration correspondingly with the temperature, but its effect is only temporary. In two or three hours, less in severe and obstinate cases, the tem-

perature will be as high as before and the bath must be repeated and the process *must be continued as long and as often as the temperature approaches a dangerous point.*

This treatment should be inaugurated and superintended by the physician in person. If the baths are administered by inexperienced nurses more harm may be done than good accomplished, for the baths stimulate the heat producing functions of the body, and unless the abstraction is thorough the good effect will in this way be counteracted. The nurses must be instructed thoroughly in the discharge of their duties. They must be taught how to take observations of the temperature with the clinical thermometer; in bad cases it should be used hourly and the result recorded for the information of the medical attendant. They must be taught how to temper the bath and cool it down, which must be done by rapidly drawing off the water as it is warmed by the abstraction of the heat from the patient's body, and adding cold water. I have seen the temperature of the water in the bath-tub rise five or six degrees in less than that many minutes, so rapid is the abstraction. Nurses of ordinary intelligence will soon master the situation.

As soon as the diagnosis is well established, or



before, if hyperpyrexia is an element of danger, (for this treatment is appropriate for all diseases characterized by high temperature), this treatment should be begun. As soon as the temperature of the patient in the axilla reaches 103° F. a full length bath should be administered and repeated as often as the temperature reaches that point. It may require a dozen or more baths per day in obstinate cases during the first few days of the fever. This treatment, even thus early in any given case, has to a certain extent a prognostic value; for, if during the first week, we have a patient with an extremely high temperature which is controlled with difficulty we may confidently expect a severe case during the second and third weeks. Although these baths in most cases are agreeable to the patient, they sometimes become irksome and distasteful long before the necessity for them ceases; fortunately we possess an article in that much abused drug, Sulph. Quinia, which *supplements the action of the water and obviates the necessity for such frequent repetition of it.* If given at the proper time and in sufficient quantity it not only produces a full and complete *remission*, but prolongs it until the following day is well advanced, even in the early stages of this disease, and renders the bath unnecessary during the latter period of the

case. So far as our present knowledge extends the sulph. quinia is by far the most valuable article in the *materia medica* for lowering temperature in hyperpyretic conditions, yet it has no power to cut short the disease, at least in doses which can safely be used. But in order to accomplish a good result it must be administered with an unsparing hand and *at the proper time of day*, for little or no good will be accomplished by giving it in small portions scattered throughout the twenty-four hours. It is folly to give it in any quantity *in the morning* in order to prevent the *evening exacerbation*, for it cannot be done in this disease. The patient will suffer all the inconveniences of the remedy with no corresponding benefit. But, on the contrary, if it is given in one full dose of from 25 grs. to 50 grs. *in the early evening* it will strike the morning remission with the full force of the remedy, and the consequence will be that the temperature *will approach the normal closely*, and in the latter stages of the disease fall below with a cessation of all the dangerous symptoms which may have been present. This remission will continue from twelve to forty-eight hours, according to the obstinacy of the particular case or the period of disease at which it is administered, allowing time for the vital organs to cool off, thus preventing the conges-

tions, inflammations and degenerations of tissue which is undoubtedly the cause of the heavy mortality of this disease. Quinia given in this way does not produce the unpleasant effects so often seen to follow the administration of small doses continued for several days. It is the *tonic* and not the *sedative* dose which produces the unpleasant cinchonism. No harm has ever been known to result from its use in this way. Liebermeister has administered it over ten thousand times by this method, giving as much as forty-five grains at a single dose. Jurgensen gives seventy-seven grains as his maximum dose, and I have administered as much as seventy-two grains at a single portion. I have now administered this remedy in antipyretic doses about fifteen hundred times with no unpleasant effects, save a transient cinchonism, and when given in the evening the patient usually sleeps through this.

The changes produced in the appearance of a patient by this treatment are certainly remarkable. The disease is temporarily deprived of all those symptoms which we are accustomed to see in typhoid fever; and when the treatment is begun sufficiently early they fail to make their appearance. The low muttering delirium is gone, the hot dry skin, which we are accustomed to see, is bathed in a profuse perspiration; the frequent

and feeble pulse of 120 or 130 drops to 75 or 80 per minute, is full and soft ; the tongue moistens with each remission, meteorism fails to appear or rapidly subsides under the influence of the bath or the quinia. The latter seldom fails to move the bowels several times each day subsequent to its administration and large quantities of fecal matter and flatus, which ought to be, are expelled, and the unabsorbed portion of the quinia thoroughly disinfects these discharges and contributes something toward preventing the spread of the disease.

Patients treated upon this plan *retain their consciousness* throughout the disease. They take an interest in surrounding events. They can describe all their subjective symptoms. They soon recognize the unpleasant effects of high temperature from their own sensations. They ask frequently for a repetition of the bath before the physician deems it advisable to use it. They beg for the administration of the quinia every day instead of each alternate day.

It will readily be seen what an immense advantage in the struggle for life a patient in this condition will have over his fellow whose intellect is muddled and rendered obtuse by the typhoid condition, and how much easier it is for the physician to detect and counteract the dangers of

secondary lesions and intercurrent affections which are so fatal in this disease.

The application of the cold water simply abstracts the heat and does not interfere with the rapid oxidation of the tissues which produces the hyperpyrexia; the remission is of course much shorter than that produced by the quinia, which acts chemically and to a certain extent prevents oxidation, if only by its mere presence. Its power for good may be abused and if continued too long become an element of danger. It lowers temperature by arresting molecular changes in the blood and tissues of the body, thus seriously interfering with the processes of nutrition and assimilation. The profound impression which it makes should not be continued too long nor repeated too often, for if continued from day to day it is not altogether free from danger. The full benefit to be derived from it is obtained by the remission which it produces—allowing the organism to cool off and thus preventing serious organic lesions; consequently it is not advisable to administer this medicine, as a rule, oftener than each alternate day, and frequently during the latter part of this disease, it will not be required oftener than each third or fourth day with an occasional bath in the afternoon.

It is best to begin the administration of quinia

with a 25 or 30 gr. dose. If this does not produce a satisfactory remission it should be increased until the maximum is reached for the particular case under treatment. This quantity, whatever it proves to be, can be materially reduced in the latter stages of the disease.

When this treatment is begun early, no other treatment is usually required. I am in a habit of presaging it with two or three cathartic doses of calomel; this is an efficient cathartic and clears the alimentary canal thoroughly of any accumulations of feculent matter—is a parasiticide and prevents the absorption of any further infectious material from that source and is supposed to exert a favorable influence upon the subsequent course of the disease. It should not be administered *after* the typhoid condition is thoroughly developed for reasons which are sufficiently obvious without any explanation. Occasionally a case will occur where the baths and quinia do not produce satisfactory remissions. In these cases the administration of the quinia should be preceded by digitalis or veratria for a period of twenty-four or thirty-six hours. I have met but two cases of this kind out of sixty-three, in both of which a full dose of 45 grs. quinia following the digitalis was entirely satisfactory. Neither digitalis nor veratria should be given in



the latter stages of this diseases, for whatever may be said of the action of digitalis as a heart tonic in other diseases, it is certainly not a safe remedy in the latter weeks of typhoid fever.

To Dr. James Currie, of Liverpool, is due the credit of first using cold water scientifically for the abstraction of heat in hyperpyretic conditions. To him is due the invention of the curved axillary thermometer, one of which has been preserved in the British Museum. His method was adopted largely throughout the British Isles and on the Continent, in the English army and navy. His works were translated into French and German, and an edition was published in this country in Philadelphia. (Currie was a citizen of the colony of Virginia when the Revolutionary War broke out, but being loyal to the Crown he returned to England.) His rules for abstracting heat by water have been improved but little. Quinine had not been extracted from the bark in his day, yet he used the latter freely. The suddenness with which Currie's plan of treatment was abandoned after his death, which occurred in 1805, is one of the unexplained mysteries of medicine.

We are indebted to the Germans for reviving and establishing this plan of treatment on a sound philosophical basis. It is the most rational

as well as the most successful treatment that has ever been adopted in this fever, as is clearly shown by statistics. At Basle, Switzerland, Liebermeister reduced the death rate from 28 per cent. to 8 per cent. At Kiel under antipyretic treatment a little more vigorously and systematically applied the mortality fell to 3.1 per cent.

The analysis of the statistics of the German Army are valuable and convincing. From 1820 to 1844 the death rate was a little over 25 per cent. From 1868 to 1874, under partial and imperfect antipyretic treatment, the rate per cent. of deaths was reduced to 15. From 1874 to 1880 the treatment was more general and the death rate was reduced to 8 per cent. In the Second Army Corps the cold water treatment was more thoroughly tested. When this treatment was begun by Dr. Abel, who is a strenuous upholder of this plan, the mortality rated at 20 per cent., which, however, soon fell to less than 5 per cent. Still more striking is the confirmation afforded by the five principal hospitals of this corps which were under the immediate and personal supervision of Dr. Abel. In 1860 the mortality had been 25 per cent., by 1877 it was lowered to 7 per cent., and during the five years following the immediate coming of Dr. Abel it fell

to 14 deaths in 764 cases, or 1.8 per cent. ; these figures are taken from an article in the *Review Scientifique* from among many others all from official sources and all pointing to the same conclusion.

During an extensive epidemic which has recently prevailed in France this plan of treatment has been tried successfully in some localities, although the French, since the Franco-Prussian war, do not take kindly to German methods. In Paris the hospital physicians disagreed in regard to its utility upon theoretical grounds, and it was not used systematically and consequently gives no statistics of value. In the city of Lyons it was vigorously used, with a reduction of the mortality rate to 2 per cent.

Our most favorable reports come, however, from private practice. Neither water-works nor bath-rooms are necessary to secure the best results from this plan of treatment. Indeed, the latter cannot be used, for patients cannot be transported from the sick chamber to a bath-room, even though it might be in an adjoining apartment. I have treated upon this plan sixty-three cases with two deaths. Dr. J. R. Featherstone, of Indianapolis, has treated fifty-seven cases with one death. Dr. W. H. Vanzant, of Carbon, Ind., has treated twenty-six cases with

no deaths. Dr. S. E. Earp, of Indianapolis, has treated eleven cases with no deaths. This gives a total of (157) one hundred and fifty-seven cases with three deaths only, or a rate per cent. of mortality of 1.9.

The highest temperature reached by any of these cases was  $107.75^{\circ}$ . It occurred during the death agony after severe and repeated hemorrhages in a patient whose temperature previous to that time had not exceeded  $104.5^{\circ}$ . One patient recovered whose temperature about the middle of the second week touched  $107.5^{\circ}$ , another whose temperature reached  $107^{\circ}$  recovered. The temperature of sixteen of my cases went to  $106^{\circ}$  and beyond, some ranging as high as  $107.5^{\circ}$ —all of these recovered, a result hardly to be expected from any other plan of treatment.

Hemorrhage of the bowels occurred in nine cases, or a little less than six (5.7) per cent. It has been claimed that hemorrhages are more frequent under this plan of treatment. Exactly the converse is true. The inflammation is less in the ulcerated mucous membrane, the bowel is not stretched and distended, and its capillaries torn by tympanitis. This is one of the complications which belongs more properly to the latter stages of the disease. More patients live to the period of the disease at which it occurs, which accounts

for the apparent increase in the number of cases suffering from this accident.

Of these one hundred and fifty-seven cases, eight relapsed, five and two-tenths per cent. of the whole. It is also claimed by the opponents of this plan that more relapses occur than when the expectant or do-nothing plan of treatment is adopted. It would be strange, indeed, if this were not true, twenty additional lives are saved out of each hundred treated by this method as compared with the expectant treatment. So the relapses ought to be one-fifth greater, having that much more material out of which relapses are liable to occur, while the 20 per cent. of dead under the expectant treatment can furnish none.

Sixteen of Dr. Vanzant's cases were treated by affusion and ten by immersion. Three of the former relapsed. His largest dose of quinia was fifty grs.

Drs. Featherstone's and Earp's cases were treated by sponging, the cold pack, and an occasional bath. The largest dose of quinia administered by the former was sixty grs., the latter fifty grs. All the cases which I have treated since 1878 have been immersed with the exception of my last case, which was treated by affusion. I find that the water and quinia supplement the action of each other. The intermission produced by the quinia after the use of the bath is much more satisfactory and prolonged, while the quinia renders the necessity for the bath much less frequent.

The case which I treated by affusion was a healthy male adult aged 19. He was the last one of eight cases which made their appearance in a club of Asbury students. The attack promised to be unusually severe, the temperature ascending to  $105^{\circ}$  Farh. on the afternoon of the fourth day. At 3 p.m. he was stripped and placed in a large tub in the erect position and about five gallons of water, the temperature of which was  $75^{\circ}$ , poured slowly over his body. Fifteen minutes afterwards his temperature was  $99^{\circ}$ . At 7 p.m. his temperature had risen to  $105.5^{\circ}$ , when the affusion was repeated with a similar result. Forty grains of quinia were administered at the same time. The patient perspired profusely through the night, slept well, and on the following morning at 8 a.m. temperature normal, pulse 76, respiration 20. This condition continued for about thirty-six hours when the temperature gradually arose, but never exceeded  $102.5^{\circ}$  during the remainder of the disease. After this period of the disease had passed, 15 grs. of quinia produced a perfect remission, and no more water was used, but the duration of the fever was twenty-six days. Affusion should be used only during *the first few days of the fever.*

Patients treated upon this plan have few or no sequelæ and are able to resume their occupations in a few days after convalescence is established.

Few conditions arise which contra-indicate its use: of course that perfect degree of rest necessary in hemorrhage and perforation forbids its employment in cases where these complications arise.

Greencastle, Ind., September, 1883.





